REMARKS

Claims 1-3, 7-10, 14-16, 18, 19, 21, 22, 24 and 26 are pending in the application. Claims 1-3, 7-10, 14-16, 18, 19, 21, 22, 24 and 26 were rejected. Claims 4-6, 11-13, 17, 20, 23 and 25 were subject to a restriction requirement and were canceled in the prosecution. No claims have been allowed.

Claim Rejections- 35 U.S.C. §103

1. Claims 1-2, 7-9, 14-16, 18-19 and 21 were rejected under 35 U.S.C. §103(a) as being unpatentable over Kim *et al.* (*Biosensors & Bioelectronics* (2000), vol. 14, pp. 907-915) in view of Sigal *et al.* (U.S. Patent No. 6,319,670 B1).

Kim *et al.* discloses a conductimetric membrane strip immunosensor for the detection of human serum albumin (HSA) as an analyte. Kim *et al.* teaches the use of antibodies against the HSA analyte which have been conjugated to colloidal gold particles as a signal generator for the conductimetric immunosensor. Kim *et al.* teaches first to affinity purify antibodies against human serum albumin (HSA) and then to conjugate the

affinity purified antibodies with colloidal gold particles. Kim *et al.* adds polyaniline strands to the gold particles to improve electrical conduction.

Sigal *et al.* disclose methods for performing electrochemiluminescence assays using electrically conductive microparticles having a first assay-ligand (such as an antibody) immobilized on it surface. A second assay-ligand (such as an antibody) is immobilized on an electrode surface. The antibodies can each bind an analyte of interest so as to form a complex, thereby binding the electrically conductive complex to the electrode surface. Thus, the conductive microparticles are bound directly to the electrodes. Sigal *et al.* do not teach a biosensor device similar to the claimed invention.

Independent claims 1, 7, 8 and 14 have been amended to limit the conductive polymer to "an electrically conductive polymer formed by oxidative polymerization of monomers, and the polymer has been mixed to react with the second capture reagent, wherein there is an absence of electrically conductive particles". Support for forming the polymer by oxidative

polymerization of monomers, and the polymer mixed to react with the second capture reagent is found at page 16, lines 11-20 of the specification. Support for an electrically conductive polymer wherein there is an absence of electrically conductive particles is provided at page 2, lines 8-10 of the specification. The claim language limits the conductive polymers to non-particulate polymers, *ie.* formed in absence of conductive particles and formed by polymerization of monomers. Kim *et al.* also synthesized polyaniline by oxidative polymerization (Kim *et al.*: page 909, left column, first full paragraph, citing Sergeyeva *et al.* (1996) and Sergeeva *et al.*, enclosed herein) to form "strands" of polymer (Kim *et al.*: page 913, last paragraph and page 914, first full paragraph) as "extended filaments" (Kim *et al.*: page 913, right column, last paragraph). Thus, it is clear that conductive polymers formed by oxidative polymerization of monomers are not particulate, but are extended filaments. However, while Kim *et al.* uses polyaniline as the polymeric conductor molecule, Kim *et al.* introduced the polymeric conductor molecules on the particulate gold surface after combining the antibody

solution with the gold particles for conjugation. (Kim *et al.*: page 909, left column, first full paragraph).

In addition, it is improper to combine references where the references teach away from their combination. *In re Grasselli*, 713 F.2d 731, 743, 218 USPQ 769, 779 (Fed. Cir. 1983). Kim *et al.* teach the strategy of using the colloidal gold-antibody conjugates with the conducting polymer and not the direct labeling of the antibody with the conducting polymer by chemical reaction "because, in such a case, the protein molecule itself does not contain available sites for electron relay." (Kim *et al.*: Conclusions, page 914). Therefore, one skilled in the art reading Kim *et al.* would be directed away from eliminating the metal (gold) particles since Kim *et al.* teaches that direct labeling of the antibody with the polymer would not have the electron relay sites on the antibody protein molecule which are necessary for conduction. Therefore, Kim *et al.* and Sigal *et al.*, either taken alone or in combination, do not show or suggest the biosensor device and system of the presently amended claims. Reconsideration of the rejection is requested.

2. Claims 3, 10, 22, 24 and 26 were rejected under 35 U.S.C. §103(a) as being unpatentable over Kim *et al.* (*Biosensors & Bioelectronics* (2000), vol. 14, pp. 907-915) in view of Sigal *et al.* (U.S. Patent No. 6,319,670 B1) as applied to Claims 1, 8 and 14, and further in view of Roberts *et al.* (U.S. Patent No. 5,958,791).

Newly amended Claims 22, 24 and 26 are directed to multi-array detection as a multiple array of first zones each having a first capture reagent with a different specificity to immobilize one of multiple analytes on the strip of substrate so that the multiple analytes can be detected simultaneously from the sample. Support for this is found on page 11, lines 19-25 and on page 19, lines 15-22 of the specification. Claim 26 has been further amended such that the multiple analytes can be detected simultaneously from the sample by providing a constant current and measuring generated voltages across the area of each of the first zones. Support for this is found on page 19, lines 22-29 of the specification.

Claims 3, 10, 22, 24 and 26 are patentable over Kim *et al.* and Sigal *et al.* for the reasons discussed

above. Additionally, with regards to Claims 22, 24 and 26, Kim *et al.* and Sigal *et al.* further fail to teach a multiple array of first zones as claimed, so that multiple analytes are detected simultaneously in the same sample. Roberts *et al.* teaches test devices including multiple sets of interdigitated electrode arrays for simultaneous multiple analyte detection and assay of a test sample for a plurality of analytes. However, Roberts *et al.* does not teach a multiple array on a single strip of substrate as taught by Applicants as illustrated in Figure 3. The simultaneous multiple analyte detection taught by Roberts *et al.* uses multiple sets of interdigitated electrode arrays in order to perform simultaneous multiple analyte detection to assay the test sample for a plurality of analytes. The liposome-enhanced immunoassay and test device taught by Roberts *et al.* would not suggest to a person of ordinary skill in the art the single multiple array as taught by Applicants, since the nature of the immunoassay and test device taught by Roberts *et al.* requires separate competitive binding portions 104 and measurement portions 106. The test of Roberts *et al.* requires that a test mixture with the analyte of interest

first passes through a competitive binding portion 104 having the binding material for the analyte before passing through a liposome lysing portion 106 where a liposome lysing agent releases the electroactive marker from the liposome. The electroactive marker is then carried by the migrating mixtures, via capillary action, into and through the electrochemical measurement portion to complete the electrical circuit (Roberts *et al.*: col. 15, line 53 through col. 16, line 5). A multiple array on a strip of substrate as claimed by Applicants (seen illustrated in Figure 3) wherein a plurality of analytes in a mixture can each be individually detected at one of the multiple regions 21A to 21D would not be suggested by the cited prior art references. As seen in Figure 3, each one of the analytes bind to a specific capture reagent/antibody at one of the multiple zones between the electrodes to generate a signal at one of the regions 21A-21E representative of that particular analyte. Each analyte will generate one of an array of simultaneous voltage signals 33 which is proportional to the change of the resistance in that region. The immunoassay and test device taught by Roberts *et al.* does not show or suggest

such an array, since specific binding must be completed *before* the test mixture flows between the electrodes in the measurement portion 106. If the adjacent electrodes are spaced too closely together in the immunoassay and test device taught by Roberts *et al.*, the electroactive marker diffuses over to an adjacent region to generate a false signal in that region. Due to this problem, the electrode arrays of Roberts *et al.*, unlike those arrays taught by Applicants, must be maintained at a large enough distance so that no electroactive markers can diffuse over the electrodes in an adjacent measurement portion 106. This is the reason that a single strip of substrate is not used. The design of the device taught by Applicants does not have this problem with cross over signal. Since only the first capture reagent specific for the desired analyte is present between the electrodes only the desired complex of the analyte and second capture reagent bound to the electrically conductive polymer can be bound between the electrodes. Therefore any signal measured across the electrodes of any of the regions 21A to 21D is generated by specific binding of the desired analyte to the region. Reconsideration of

the rejection is requested.

In light of the above, it is now believed that Claims 1-3, 7-10, 14-16, 18, 19, 21, 22, 24 and 26 are patentable and in condition suitable for allowance. Applicant respectfully requests that a timely Notice of Allowance be issued in this case.

Respectfully submitted,

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Enclosures:
Declaration under 37 C.F.R. §1.132.
Sergeyeva *et al. Sensors and Actuators* B34 (1996) 283-8.
Sergeeva *et al. J. Anal. Chem.* 51(4) 1996 394-6.